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(54) Title: TOPICAL PEDICULICIDAL COMPOSITIONS

(57) Abstract

The invention provides a topical pediculicidal composition for the treatment of human and animal and other arthropod ectoparasites comprising an insecticidally effective amount of at least one active ingredient in combination with a bioadhesive cationic polymer, having affinity for the hair and providing retention of the active ingredient in the hair.

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Topical Pediculicidal Compositions

The present invention relates to a topical pediculicidal composition. More particularly, the present invention relates to a topical pediculicidal composition with prolonged residual activity for the treatment of lice and other ectoparasites.

Head lice infestation (Pediculosis capitis) has become a great burden to our society. Lice infestation is more prevalent among children than all other childhood communicable diseases combined. Despite the introduction of effective insecticides, the number of cases of lice infestation has increased worldwide since the mid-1960s (see, e.g. Gratz. N. 1977. Epidemiology of Louse Infestations, pp. 157-167. In M. Orkin, H.I. Maibach, L.C. Parish, and R.M. Schwartzman [eds.], Scabies and Pediculosis. Lippincott, Philadelphia), reaching hundreds of millions yearly, as described e.g., by Taplin, D. and T.L. Meinking. 1987. Pyrethrins and Pyrethroids for the Treatment of Scabies and Pediculosis. Semin. Dermatol. 6:125-135. Although most infested people live in poor hygienic conditions, head lice infestations are very common among children in developed countries. About 6-12 million people, mainly children, are affected annually with lice in the U.S. In Israel, in the past 20-25 yr., 15-20% of all children between 4 and 13 yr. were infested annually with head lice. In another 25-30% of the children signs of previous lice infestations e.g., dead or empty eggs (nits) were found, (as described by Mumcuoglu, et al. 1990. Epidemiological studies on head lice infestation in Israel: parasitological examination of children. Int. J. Dermatol. 29: 502-506).

Lice are obligate parasites, spending their entire life on the humans and feeding exclusively on blood. Although any part of the scalp may be

colonized, lice favor the nape of the neck and the area behind the ears, where the eggs are usually laid. Normally head lice infest a new host only by close contact, making social contacts among children and parent-child interactions a much more likely route of infestation than shared combs, brushes, towels, clothing, bed or closets. The number of children per family, sharing of beds, hair washing habits, health care in the school and socio-economic status were found to be significant factors in head louse infestation. The most characteristic symptom of infestation is pruritus on the head, which may begin 1-4 weeks after the initial infestation. The itch-scratch cycle can lead to secondary infection with impetigo and pyoderma. Although the head louse does not cause severe clinical symptoms and is not known to transfer pathogenic organisms, the psychological effects in children, parents and teachers are significant.

Several chemical agents have been used in the last decades for the treatment of pediculosis. The usual consideration for the clinician in choosing such agents is to balance the efficacy of the product against the safety, with the latter carrying much more weight. Today, four types of insecticides are being used to control lice:

(a) Carbamates: The only active ingredient being used today of the carbamates is carbaryl which is applied at 0.5% concentration in shampoo or lotion formulations. Lotions, even though not very compliant, are generally more effective since the contact time is longer. Recently, lice have been found to develop resistance to this insecticide, and therefore rotation with malathion during treatment has been suggested (Martindale, The Extra Pharmacopeia. 1993. 30th edition, J.E.F. Reynolds (ed.). The Pharmaceutical Press, London. In 1995 the British Medicines Control Agency proposed to

add carbaryl-based pediculicides to the list of drugs to be sold by prescription. This decision was based on reports that carbaryl was found to be a potential carcinogen (see Anonymous 1995. POM-to-P shift proposed for budesonide and P-to-POM for carbaryl. Pharmac. J. 255: 138).

(b) Organochlorines: DDT was widely used in the past, but because of persistence in humans has been banned in most countries. Pediculicides containing 1% lindane (Kwell, R&C Co., USA) are still in pharmacies, however the drug's label warns that neurotoxicity is possible among certain patients, especially children. Acute lindane toxicity resulting from topical application has occurred in the pediatric and geriatric populations, as reported by Fischer, T.F. 1994. Lindane toxicity in a 24-year-old woman Ann. Emerg. Med. 24: 972-974. In addition, resistant strains of head lice to lindane have been developed in recent years.

(c) Organophosphates: These are potent cholinesterase inhibitors which can be very toxic since the inhibition results in both muscarinic and nicotinic effects. One of the organophosphates, malathion, is being used for control of lice in 0.5% and 1% concentrations in shampoo and lotion formulations (Prioderm, Napp Lab., Cambridge; Monocide, Fischer Ltd. Tel-Aviv). These products are no longer available in the U.S. due to the severe irritation of the eyes and mucous membranes.

(d) Pyrethrins and pyrethroids: The insecticidal properties of the plant *Chrysanthemum* have been known for several centuries. The active ingredients e.g. the pyrethrins, were extracted during this century. They are being used in many of the over-the-counter pediculicides around the world (Pyracide and T-Pal, Fischer Ltd.; A-200, SKB; RID, Pfizer). They

decompose quickly when exposed to light and air, have low toxicity and a high knock-down effect. Some cases of contact dermatitis were reported after use of pyrethrum containing pediculicides. The synthetic pyrethrins and the pyrethroids, such as permethrin and phenothrin, are the most commercially used pediculicides in the world today for the control of lice. Permethrin has a long lasting residual activity and may remain on the hair for several weeks, killing all lice which hatch from the eggs. Resistance of head lice to permethrin has been reported from Israel, the Czech Republic, France, Great Britain and the United States (see e.g. Mumcuoglu et al. 1995. Permethrin resistance in the head louse *Pediculus humanus capitis* from Israel. Med. Vet. Entomol. 9: 427-432). People allergic to the *Chrysanthemum* plants may develop local allergic reactions to the pyrethroids as well. Most of the pyrethrum and pyrethroid-based pediculicides are being used together with the synergist piperonyl butoxide. Cross-resistance between permethrin and phenothrin has been reported from Israel and some European countries (see Mumcuoglu 1995 ibid).

Tables I and II summarize the pediculicides used today in Israel and U.S.

Table I: Pediculicides in Israel (1995)

Table I

Commercial Products for Pediculosis in Israeli Market

Active ingredient	%	Formulation	Trade Name	Company	Treatment
Pyrethrin	0.33	Gel Shampoo	A-200 Pyrinate	Mediline	Apply for 10 min. Repeat after 5 days
Pyrethrin	0.33	Shampoo	Pyracide	Fischer	Apply for 10 min. Repeat after 10 days
Pyrethrin	0.3	Shampoo	T-Pal	Fischer	Apply for 10 min. Repeat after 5 and 10 days
Pyrethrin Petroleum oil	1.33 32.7	Spray	Kin Soff	Chemipal	Apply once for 30 min For pubic lice only!
Bioallethrin Petroleum oil	0.66 33.3	Spray	Kin-X-Spray	Chemipal	Apply once for 30 min
Bioallethrin Petroleum oil	0.3 27.9	Spray	Biolkene	Princifarm Kalir	Apply once for 30 min
Permethrin	1	Cream rinse	Nok	CTS Novis (Meditrent)	Apply once for 10 min
Permethrin	1	Cream rinse	Zehu-Ze	Abic/Teva	Apply once for 10 min
Carbaryl	0.5	Lotion	Hafif-New	Abic	Apply once for 2 hrs
Carbaryl	0.5	Lotion	Carbacide	Fischer	Apply once for 2 hrs
Carbaryl	0.5	Lotion	Clinicide	De Witt/Agis	—
Malathion Allethrin	0.4 0.1	Solution	Monocide	Fischer	Apply once for 5-7 hrs
Malathion	1	Cream Shampoo	Prioderm	Napp/Rafa	Apply for 2 x 5 min. Repeat after 3 and 6 days.
Malathion	1	Lotion	Nouryl	Chefaro	—

Table II

Commercial Products for pediculosis in the US (PDR 1994)

Product	Active agent/s	Conc.	Company	Dosage form
A-200 Lice control	synthetic pyrethroid (patent)	0.5%	SKB	spray
A-200$_1$ Pediculicide	Pyrethrins Piperonyl butoxide tech.	0.3% 3.0%	SKB	shampoo
RID Lice Control	Permethrin	0.5%	Pfizer	spray
RID Lice Killing	Pyrethrins Piperonyl butoxide	0.33% 4.00%	Pfizer	shampoo
Nix	Permethrin	1.0%	Wellcome	creme rinse

While many available agents show good pediculicidal activity, most of them have a poor ovicidal ability. Except for malathion lotion, all of the products tested left more than one-fifth of the eggs viable after treatment (see Martindale, The extra Pharmacopeia. 1993. 30th edition, J.E.F. Reynolds (ed.). The Pharmaceutical Press; London). This means that most of the over-the-counter products are not fully effective. The poor ovicidal activity can be explained by the low penetration of the agents through the egg wall. This hypothesis was supported by the high rate of eggs still hatched after treatment (23%-32%) and most importantly by the existence of non-viable stillborn lice nymphs (18%-34%). This suggests that the agents principally kill only lice that have hatched from eggs, and therefore repeating treatment a week and two weeks later is necessary. However, since this treatment

regimen enables eggs to hatch for a relatively long period of time before massive killing is performed, reinfestation often occurs. Therefore, a more controlled treatment of this communicable disease's life cycle is needed.

With this state of the art in mind, the present invention provides what will be referred to as a prolonged acting system (hereinafter PAS) that suppresses the distribution of lice by the immediate killing of nymphs the moment they hatch from the eggs. The novel system of the present invention is created and formulated by using a selected series of polymers which are able to adhere to the surface of the hair and release trapped agents (e.g., pyrethrins) in a continuous manner for a minimum of 2-3 days. Alternatively and preferably, the agent is designed to constantly remain on the hair until removed by a regular shampooing. The proposed treatment concept reduces the acute toxicity of the agent, in fact, by a decrease in close-contact of the applied agent with the skin. The reduction in side effects, as well as the introduction of cosmetically elegant formulations, increase the compliance of the public to the novel product, and may lower the prevalence of the epidemic eruptions in our society.

Formulations are preferably indicated for hair treatment and they are selected from the group consisting of shampoos (liquid or gel), hair sprays, mousses, creme rinses, conditioning shampoos or shampoo conditioners, lotions, and aerosol foams. Shampoo and conditioning shampoo formulations are preferable to other hair preparations since they are applied for a shorter time and used instead of regular shampooing of the hair.

Thus, the present invention provides a topical pediculicidal composition for the treatment of human and animal lice and other arthropod

ectoparasites comprising an insecticide and a bioadhesive cationic polymer, having affinity for the hair and providing retention of the insecticide in the hair.

The compositions of the present invention preferably comprise about 0.01% to 20% (w/w) of the insecticidal agents (e.g., carbamates, organochlorines, organophosphates, pyrethrins or pyrethroids). Preferably, these agents do not exceed the recommended concentrations as approved by the health or veterinary authorities.

The compositions of the present invention further preferably comprise about 0.1%-10% (w/w) of the appropriate hair-substantive polymers that may be selected from the groups of polyacrylates, polymethacrylates, polyethylene glycols, or polysaccharides. Thus, e.g. cationic cellulose derivatives and the quaternized acrylic copolymers may be used. A strongly cationic cellulose derivative known as UCARE® Polymers JR, SR, LR (CTFA adopted name: Polyquaternium 10) are being marketed by Union Carbide Corp. (US Patents 3,472,840 and 3,816,616) as a conditioning agent in anionic shampoos. They are obtained by reaction of hydroxyethylcellulose with epichlorohydrin followed by quaternization by trimethylamine. Other quaternized polymers can also be utilized, such as those that provide wave-retention properties, as well as manageability and combability to the hair. Of these polymers, several acrylic types are exemplified:

1. dimethylsulphate quaternized poly(diethylaminoethylmethacrylate) (US Patent 3,313,734 - Procter and Gamble Co.),

2. phosphate salts of polyacrylic acid aminoethylester (US Patent 4,009,256 - National Starch and Chemical Corp.) including the related copolymers,

3. dimethylsulphate quaternized copolymers of vinylpyrrolidone and dimethylaminoethyl methacrylate (CTFA: Polyquaternium 11) also known as GAFQUAT 734, 755 copolymers,

4. Eudragit RL or RS (Roehm GmbH) are a family of polymers based on quaternary ammonium derivatives of methacrylic acids suitable for use in orally administered drug delivery systems, so they are pharmaceutically graded. The copolymers comply to "Ammonio Methacrylate Copolymer, Type B" in the National Formulary (USP/NF). They are available in a number of different grades possessing a range of physico-chemical properties.

There are also other polymers possessing high-affinity to the hair which do not belong to the above groups, but which, nevertheless, are suitable for use in the present invention. For example, these include cationic polymers derived from piperazine (US Patents 3,917,817 and 4,013,787 - L'Oreal), condensation products of polyamines with bifunctional polyalkyleneglycols derivatives in the presence of epichlorohydrin (US Patent 3,987,162), or proteins, preferably hydrolyzed collagen, with quaternized derivatives (the kind used for curl retention and wet combing).

It should be noted, that by the term "comprising" as used in the present invention is meant that various other inactive ingredients, compatible agents and drugs can be employed in the compositions as long as a critical bioadhesive cationic polymer (or several) is present in the compositions and is used in the manner disclosed.

As will be realized, the bioadhesive polymers of the compositions of the present invention serve to coat the hair and/or fur of the mammal being treated, as well as coating the eggs of the lice and/or other ectoparasites adhering thereto with the insecticidal active ingredient trapped therein, and as said eggs hatch said insecticidal active ingredient immediately kills the emerging nymphs.

Obviously, by methods known per se, said active ingredient could also be incorporated in microcapsules formed from said bioadhesive polymers, rather than merely being retained and trapped in a coating film formed thereby.

The compositions of the present invention may further comprise of either anionic, cationic, amphoteric, nonionic surfactants, or combinations thereof, especially those having a good compatibility with cationics. The anionic surfactants can be selected from: (a) alkyl sulphates such as sodium lauryl or myristyl sulphate, ammonium lauryl sulphate, or mono- and tri-ethanolamine lauryl sulphates; (b) alkyl ether sulphates such as sodium or magnesium lauryl ether sulphate; or (c) acyl sarcosinates such as sodium lauryl sarcosinate. The cationic surfactants can be the quaternized fatty acid amides. The amphoteric surfactants, by having the advantage of being compatible with both anionic and cationic surfactants, can be selected from betaines such as amidobetaine, from N-alkyl amino acids such as sodium cocaminopropionate (DERIPHAT), or from alkyl imidazolines such as MIRANOLS. The nonionic surfactants can be preferably selected from the fatty acid alkylamides such as cocamide diethylamide (LAURAMIDE R), from the poloxamers known also as Pluronics, or from the amine oxides such as cocamidopropylamine oxide (REWOMINOX B-204).

Other additives can be included in the PAS's, such as foam boosters, thickening agents, oils, sequestering agents, antioxidants, sunscreens, perfumes, colors, preservatives, and agents that form opacity, pearl-like appearance, or clarity.

An especially preferred formulation for the treatment of pediculosis comprises about 0.3% pyrethrins, about 3% piperonyl butoxide, about 1-2% POLYMER JR, about 37% MIRANOL C2MSF (amphoteric), about 2% LAURAMIDE R (nonionic), and about 5% propylene glycol in aqueous solution adjusted to pH 6-7.

While the invention will now be described in connection with certain preferred embodiments in the following examples and with reference to the attached figures, so that aspects thereof may be more fully understood and appreciated, it is not intended to limit the invention to these particular embodiments. On the contrary, it is intended to cover all alternatives, modifications and equivalents as may be included within the scope of the invention as defined by the appended claims. Thus, the following examples which include preferred embodiments will serve to illustrate the practice of this invention, it being understood that the particulars shown are by way of example and for purposes of illustrative discussion of preferred embodiments of the present invention only and are presented in the cause of providing what is believed to be the most useful and readily understood description of formulation procedures as well as of the principles and conceptual aspects of the invention.

In the drawings:

Fig. 1 is a graphical representation of hair-uptake of pyrethrins after washing with various pediculicidal shampoos.

FIG. 2 is a graphical representation of hair-uptake of piperonyl butoxide after washing with various pediculicidal shampoos.

Table III: Examples 1-6

Shampoo bases containing mostly anionic surfactants

Experiment Number

Ingredients	#1	#2	#3	#4	#5	#6
	(%)	(%)	(%)	(%)	(%)	(%)
Pyrethrins	0.3	—	0.3	0.3	0.3	0.3
Piperonyl butoxide	3	—	3	3	3	3
Permethrin	—	1	—	—	—	—
Ammonium Lauryl sulphate	30	30	30	30	30	30
Ammonium lauryl ether sulphate (25% EO)	20	20	20	20	20	20
LAURAMIDE ME (R)	2.5	2.5	2.5	2.5	2.5	2.5
Betaine	10	10	10	10	10	10
JAGUAR C-162	2	—	—	—	—	—
POLYMER JR 30M	—	2	—	—	2	—
GAFQUAT HS-100	—	—	2	—	—	—
GAFQUAT 3272	—	—	—	2	—	—
Deionized water ad	100	100	100	100	100	100

LAURAMIDE ME (or R) = cocamide diethylamide 90% sol.

JAGUAR C-162 = CTFA: Hydroxypropyl guar hydroxypropyltrimonium chloride (Rhone-Poulenc).

POLYMER JR 30M = Polyquaternium 10 (Union Carbide Corp.)

GAFQUAT HS 100 = Polyquaternium 28 (GAF Co.)

GAFQUAT 3272 = Polyquaternium 11 (GAF Co.)

Table IV: Examples 7-9, 11-17

Shampoo bases containing mostly amphoteric surfactants

Experiment Number

Ingredients	#7	#8	#9	11*	#12	#13	#14	#15	#16	#17
	%	%	%	%	%	%	%	%	%	%
Pyrethrins	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Piperonyl butoxide	3	3	3	3	3	3	3	3	3	3
Propylene glycol	5	5	5	5	5	5	5	5	5	5
MIRANOL C2MSF	37*	37*	24.2	37	37	37	37	37	37	37
LAURAMIDE R	2	2	2	2	2	2	2	2	2	2
JAGUAR C-162	—	—	—	—	1.5	—	—	2	—	—
POLYMER JR 30M	2	1.5	—	1.5	—	—	—	—	2	—
GAFQUAT HS-100	—	—	—	—	—	—	2	—	—	—
GAFQUAT 3272	—	—	—	—	—	2	—	—	—	—
Citric acid	2	1	2	1	1	1	1	1	1	1
Deionized water ad	100	100	100	100	100	100	100	100	100	100

* Except Formulations 7 and 8, all others included "MIRANOL" manufactured by Zohar Detergent Factory (Dalia) under the name ZOHARTERIC D-SF.
MIRANOL C2M SF = Imidazoline-based surfactant (CTFA: Amphoteric 2)
LAURAMIDE ME (or R) = cocamide diethylamide 90% sol.
JAGUAR C-162 = CTFA: Hydroxypropyl guar hydroxypropyltrimonium chloride (Rhone-Poulenc).
POLYMER JR 30M = Polyquaternium 10 (Union Carbide Corp.)
GAFQUAT HS 100 = Polyquaternium 28 (GAF Co.)
GAFQUAT 3272 = Polyquaternium 11 (GAF Co.)

* Formulation #11 was repeated on scale-up batch no. **PS-19.** Batch PS-19 was tested on incubated lice comparing to **PS-21** (formulation without insecticides) as described in Example 19 (below). Formulation No. 10 was a

commercial product (Pyracide, Fischer) used as a positive control in the insecticides uptake tests.

Example 18

Uptake of Pyrethrins and Piperonyl butoxide by Hair using Various PAS's

A Comparative Study

Methodology: One gram of human hair was washed in 9 ml tap water containing 1 g of an insecticidal shampoo, at 35°C for 15 minutes. After washing, the hair was dipped twice in tap water (100 ml) for 1-2 minutes each time, thereafter the hair was taken out and well-shaken to remove any excess of water. Extraction of the insecticides from the washed hair was made with 30 ml methanol (HPLC grade) while stirring for 15 minutes. The extract was quantitatively transferred to a 100-ml volumetric flask and volume was made up with methanol.

The methanolic extract was analyzed for pyrethrins (1 and 2) and piperonyl butoxide using a HPLC assay. Aliquots of 20 ml were injected into the HPLC system, which was equipped with a prepacked C_{18} column (Lichrospher 60 RP-select B, 5mm, 125X4mm, Merck). The detection of the pyrethroids was carried out at 230 nm. The samples were chromatographed using an isocratic mobile phase consisting of acetonitrile - methanol - water (12:68:20). A flow rate of 1 ml/min was used. The data was analyzed using 1 Mg/ml pyrethrins and 1 Mg/ml piperonyl butoxide standard solutions in methanol, which were run for every series of chromatographed samples. Plots of calibration curve (peak area versus drug concentration) over the range of 0.5-10 Mg/ml pyrethrins and 1-100 Mg/ml were linear (y=88373x, r=0.999, for Pyr-1; y=121577x, r=0.999, for Pyr-2; y=31656x, r=0.999, for P.B.).

Results: Figure 1 presents the uptake of pyrethrins on the human hair using various shampoos based on cationic polymers and an amphoteric-nonionic surfactant combination (Table IV). Figure 2 shows the uptake of piperonyl butoxide on the hair after shampooing with the same formulations. It can be seen from both figures that the four polymeric formulations were superior over the commercial Pyracide product. The two pyrethrins were significantly taken up by the hair using all polymer-containing formulations as compared to the non-polymer containing shampoo. However, comparatively low quantities of piperonyl butoxide were taken up after using three of these formulations, and the uptake values obtained were probably resulted mainly by the amphoteric surfactant (Figure 2). As found and illustrated in Figures 1-2, Formulation 11 created a dramatic uptake on the hair of both the pyrethrins and the piperonyl butoxide.

In the figures the legends of the shampoos used is as follows:

Pyracide shampoo (Fischer) - Exp. #10
No polymer - Examples #9 and #17
Polymer 1 - Example #11 - POLYMER JR
Polymer 2 - Example #13 - GAFQUAT 3272
Polymer 3 - Example #14 - GAFQUAT HS-100
Polymer 4 - Example #15 - JAGUAR C-162

The uptake of insecticides by hair after shampooing with formulations 1-6 was not significantly different from the uptake on hair treated with a non-polymer containing shampoo.

Example 19

Pediculicidal Efficacy Testing with PS-19 Shampoo

A Comparative Study

The pediculicidal and ovicidal activity of a formulation was tested in our laboratory on the human body louse according to the following procedures:

Body lice (Pediculus humanus humanus) are reared in the laboratory by feeding them every second day on rabbits. Lice are placed on the shaved abdomen of a white rabbit and left until they have fed to satiety. Outside the host the lice are maintained at a temperature of 30-32°C and relative humidity of 70-80%.

For each test 50 lice (10 males, 10 females and 30 nymphs) were placed on ½ gram of human hair. The hair was previously treated for 10 min (at 35-37°C) with the test substance by dipping them in 5 ml of a 10% solution of the formulation PS19. The excess liquid was then allowed to drip off and the hair dried with a piece of cotton cloth. The lice were left in contact with the treated hair overnight at optimum temperature and humidity. Mortality was determined after 16-18 hrs. Each experiment was repeated three times. As a negative control PS 21 (the formulation without the insecticide) and regular shampoo, both diluted 1:10, were used.

In order to establish the residual activity of the product 3 g of hair were treated as described above and left in the incubator at 35°C. On day 1, 3, 5 and 8 after treatment, fresh groups of lice were placed on ½ gram of the hair and the mortality determined after 16-18 hrs. The effect of the product was also tested on laboratory animals. A 5 x 5-cm surface of rabbit fur was treated with 1.5 ml of the test solution for 10 min. The fur was then washed with 25 ml

of tap water and towel dried. After 30 min, when the hairs were thoroughly dry, 100 lice were placed on the treated area for 2 hrs. They were then transferred to a piece of filter paper in a plastic container and incubated overnight at optimum temperature and humidity. Mortality was recorded after 18 hrs.

The results of the tests can be seen in tables 1-3.

Table 1: Pediculicidal activity of PS 19

Formulation	% mortality of lice
PS 19	99.3
PS 21	4.7
Regular Shampoo	2.1

Table 2: Residual activity of PS 19 after exposure of lice to treated hair for 8 days.

Formulation	Days after treatment	% mortality of lice
PS 19	1	100
	3	100
	5	98
	8	100
PS 21	1	2.7
	3	4.1
	5	4.7
	8	4.7
Regular shampoo	1	1.3
	3	2.0
	5	2.0
	8	4.1

Table 3: Pediculicidal activity of the product on treated animals.

Formulation	% mortality of lice
PS 19	87
Regular shampoo	4

Conclusion: Following treatment of the hair for 10 min with a 10% solution of PS 19, lice which remained on the hair overnight are killed. None of the other ingredients of the formulation had any effect on lice. The insecticide remained fully active on hair for at least 8 days, if the hair was not washed with a normal shampoo.

Example 20

Pediculicidal Efficacy Testing with PS-19 Shampoo

A Comparative Study

The pediculicidal and ovicidal activity of a formulation was tested in our laboratory on the human body louse according to the following procedures:

Body lice (Pediculus humanus humanus) are reared in the laboratory by feeding them every second day on rabbits. Lice are placed on the shaved abdomen of a white rabbit and left until they have fed to satiety. Outside the host the lice are maintained at a temperature of 30-32°C and relative humidity of 70-80%.

For each test 50 lice (10 males, 10 females and 30 nymphs) were placed on ½ gram of human hair. The hair was previously treated for 10 min (at 35-37°C) with the test substance by dipping them in 5 ml of a 10% solution of the formulation PS19. The excess liquid was then allowed to drip off and the hair dried with a piece of cotton cloth. Lice were left in contact for 5, 10, 15, 30, 60, 120, 180, and 300 min. Thereafter, hair and lice were treated with shampoo for 1 min and washed with tap water for another 1 min. Mortality was determined after 16-18 hrs. Each experiment was repeated three times. As a negative control regular shampoo, diluted 1:10, and as a positive control a shampoo formulation of a pyrethrum-based pediculicide, were used.

The following table gives the results of these examinations:

Table 1: Pediculicidal activity of PS 19

Formulation	Exposure time (min)	% mortality of lice
PS 19	5	100
	10	100
	15	100
	30	100
	60	100
	120	100
	180	100
	300	100
Pyrethrum-based pediculicide	60	86.7
	120	86.7
	180	90.0
	300	90.0
Regular Shampoo	300	12.0

Conclusions: PS19 has a very potent pediculicidal activity and kills all the active stages of the lice within 5 min of exposure. As a comparison a pyrethrum-based pediculicide which is sold on the Israeli market gives about a 86.7% and 90% mortality rate only after 1 and 3 hrs, respectively.

It will be evident to those skilled in the art that the invention is not limited to the details of the foregoing illustrative examples and that the present invention may be embodied in other specific forms without departing from the essential attributes thereof, and it is therefore desired that the present embodiments and examples be considered in all respects as illustrative and not restrictive, reference being made to the appended claims, rather than to the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

WHAT IS CLAIMED IS:

1. A topical pediculicidal composition for the treatment of human and animal and other arthropod ectoparasites comprising an insecticidally effective amount of at least one active ingredient in combination with a bioadhesive cationic polymer, having affinity for the hair and providing retention of said active ingredient in the hair.

2. A topical pediculicidal composition according to claim 1, comprising about 0.01 to 20 w/w% of at least one insecticidally effective active ingredient.

3. A topical pediculicidal composition according to claim 1, wherein said active ingredient is a pyrethrin.

4. A topical pediculicidal composition according to claim 1, wherein said active ingredient is piperonyl butoxide.

5. A topical pediculicidal composition according to claim 1, wherein said active ingredient is a pyrethroid.

6. A topical pediculicidal composition according to claim 1, comprising about 0.1 to 10 w/w% of a bioadhesive cationic polymer.

Figure 1

Hair Uptake of Pyrethrins after Washing with Various Shampoos

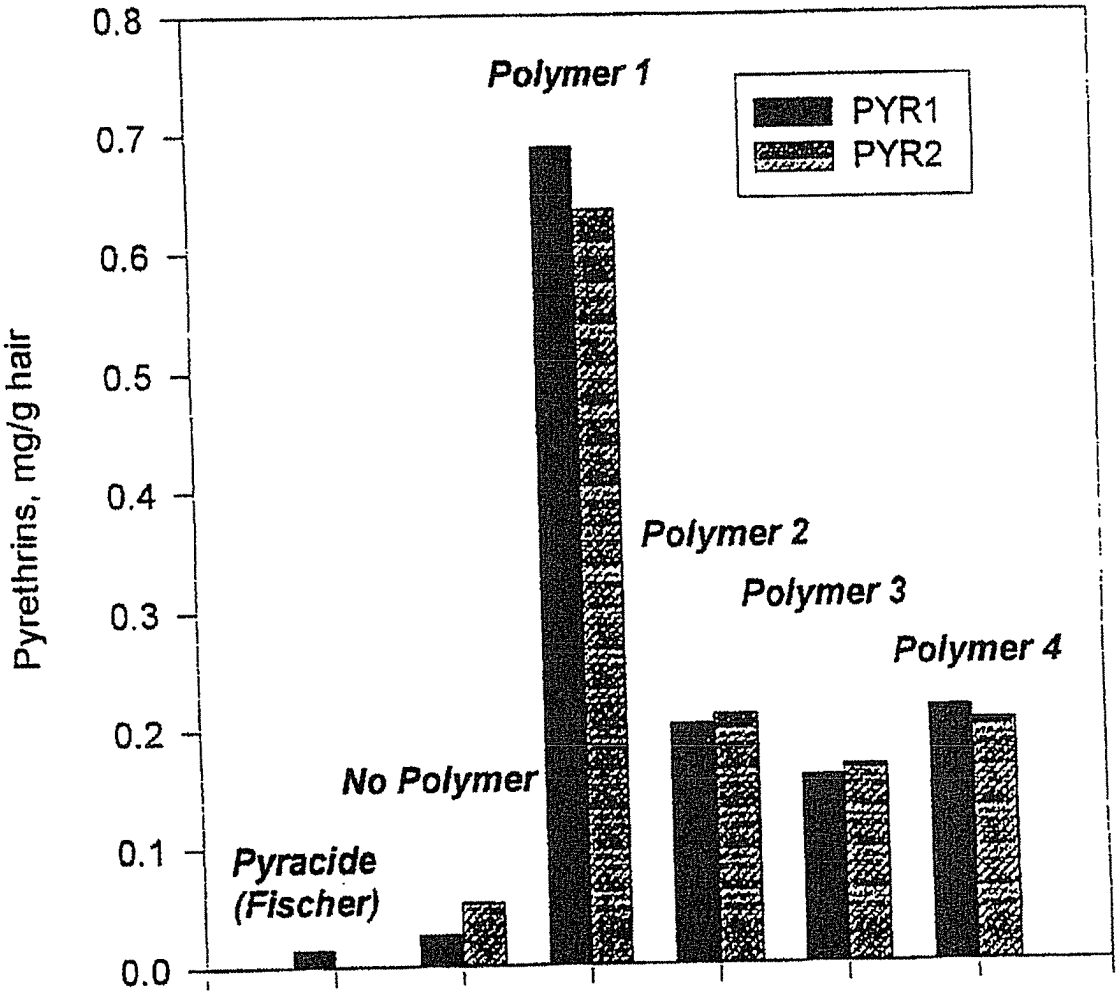
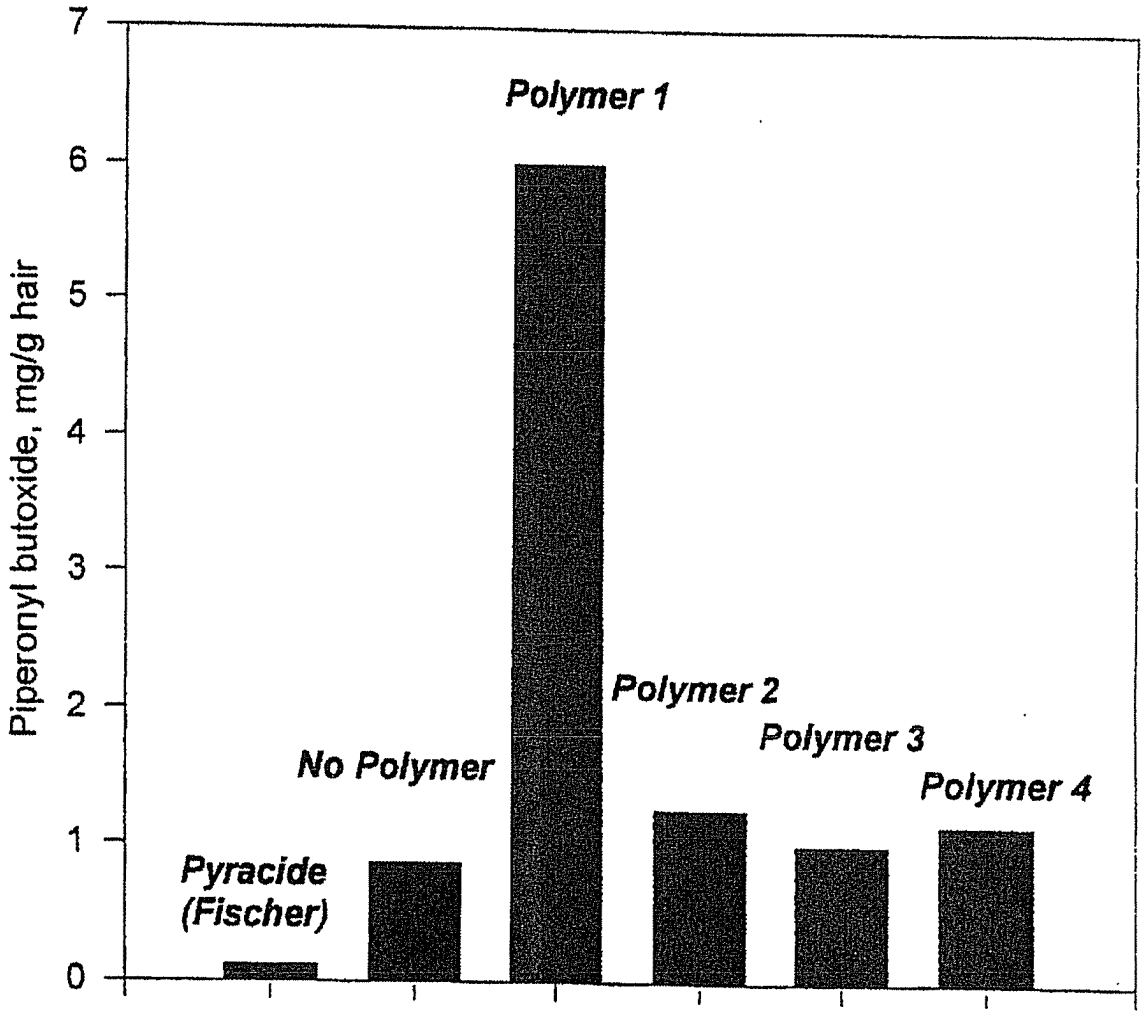


Figure 2

Hair Uptake of Piperonyl Butoxide after Washing with Various Shampoos



INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/GB 97/01434

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A01N25/24 A61K7/40 A61K7/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 117 135 A (JOHNSON&JOHNSON) 29 August 1984 see page 1 see page 3, line 11 - line 19 see page 8, line 23 - page 9, line 35 see page 10, line 20 - line 23 see page 11, line 21 - line 34 see page 13, line 11 - line 20 see example XVII see claims 1,8,9,11,12,15,16 ---	1-6
X	GB 2 222 949 A (EUROCELTIQUE S.A.) 28 March 1990 see page 1 - page 3; claims 1,7,8,16,17 --- -/--	1-6

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
5 September 1997	15.06.97

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/GB 97/01434

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 1 586 258 A (BAYER AG) 18 March 1981 see page 1 - page 2, line 9 see page 2, line 23 - line 30 see examples C,F see claim 1	1-6
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INTERNATIONAL SEARCH REPORT

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